

Please cancel claim 31.

**REMARKS**

Claim 32 covers the use of the assay of the present invention to detect the occurrence and severity of stroke (cerebrovascular accident) in a patient; cerebrovascular accident and stroke are equivalent terms (see materials attached). Antecedent basis for this claim is found in claims 14 and 30, as originally filed, as well as at page 4, line 17-page 5, line 4 of the present application.

Since the Vandermeeren et al. patent does not disclose or suggest any connection of the presence of tau protein in cerebrospinal fluid with the occurrence of cerebrovascular accident (or stroke), newly-added claim 32 is allowable thereover. Vandermeeren et al. deals only with Alzheimer's Disease.

Claim 31 has been canceled as being largely redundant of amended claim 14.

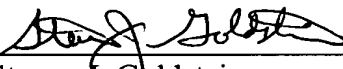
Accordingly, reconsideration of the present application and allowance of the claims currently pending therein are respectfully requested.

Respectfully submitted,  
Frank P. Zemlan et al.

**CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Box AF, The Assistant Commissioner for Patents, Washington, D.C., 20231, on March 21, 2002.

  
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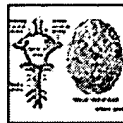
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## Stroke

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### Illustrations

[Brain](#)[Carotid stenosis, X-ray of the left artery](#)[Carotid stenosis, X-ray of the right artery](#)[Circle of Willis](#)[Right cerebral hemisphere - function](#)[Brainstem function](#)[Stroke](#)[Cerebellum - function](#)[Left cerebral hemisphere - function](#)[Endarterectomy](#)

### Alternative names [Return to top](#)

Cerebrovascular disease; CVA; Cerebrovascular accident

### Definition [Return to top](#)

A stroke is when the blood supply to any part of the brain is interrupted, resulting in tissue death and loss of brain function.

### Causes and risks [Return to top](#)

The brain requires about 20% of the body's total circulation of blood. The blood enters the brain from two carotid arteries in the neck, which branch off into multiple arteries that supply each specific area of the brain.

If blood flow in any of these arteries is interrupted for longer than a few seconds, brain cells can die, causing permanent damage. The resulting stroke-related symptoms depend on the area of the brain affected, the extent of the damage, and the cause of the stroke.

Common symptoms include changes in vision, speech, and comprehension; weakness; vertigo; loss of sensation in a part of the body; or changes in the level of consciousness.

Stroke accounts for 1 out of every 15 deaths in the United States. It is the 3rd leading cause of death in most developed countries, and the leading cause of disability in adults. The risk doubles with each decade after age 35. Stroke occurs in men more often than women.

The risk of stroke is increased by smoking, hypertension, diabetes, hyperlipidemia, and heart disease. Rarely, strokes may happen in women on birth control pills -- the risk is increased if a woman also smokes and is older than 35. Women have a higher risk of stroke during pregnancy and the weeks immediately after pregnancy. Other illnesses such as vasculitis, lupus, or high blood viscosity may contribute to stroke.

The most common cause of stroke is atherosclerosis. (See stroke secondary to atherosclerosis.) Atherosclerosis is a condition in which fatty deposits and blood platelets collect on the wall of the arteries, forming plaques. Over time, the plaques slowly begin to block the flow of blood. A plaque may block the artery enough to cause a stroke, or it may trigger a blood clot that causes a stroke.

The formation of a plaque does not always lead to a stroke. The arteries are large enough that 75% of the blood vessel can be blocked, and there will still be adequate blood flow to that area of the brain. Furthermore, there are many small connections between the arteries in the brain. If the blood flow is gradually blocked in one artery, these small connections will increase in size and "by-pass" the obstructed area. Even a totally blocked artery may not cause a stroke.

A stroke may be caused by a blood clot that forms in the brain (a thrombus) or a blood clot, piece of plaque, or other material that travels to the brain from another location (an embolism). Bleeding (hemorrhage) within the brain can, on rare occasions, cause symptoms that mimic stroke.

A stroke caused by a blood clot in the brain (a thrombus) is most common in older people, and often there is underlying atherosclerosis or diabetes. This type of stroke may occur at any time, including at rest. The person may or may not lose consciousness.

Strokes caused by embolism (a blood clot that travels to the brain) are most commonly caused by heart disorders. An embolism may also originate in the aortic arch, especially where there is atherosclerotic plaque. The blood clot travels through the bloodstream and becomes stuck in a small artery in the brain. This stroke occurs suddenly with immediate, maximum damage to the brain. Consciousness may or may not be lost.

Embolic strokes are NOT associated with activity levels and can occur at any time. Arrhythmias of the heart, such as atrial fibrillation, are often seen with this type of stroke and may be the cause of the clot. Other causes of embolic stroke include endocarditis (an infection of the heart valves), or a mechanical heart valve that may have a clot attached to it. A heart attack puts people at greater risk for having an embolic stroke.

The probable outcome is worsened if blood vessels damaged by stroke rupture and bleed (hemorrhagic stroke).

See also:

- Stroke secondary to carotid dissection (bleeding from the carotid arteries)
- Stroke secondary to carotid stenosis (narrowing of the carotid arteries)
- Stroke secondary to cocaine
- Stroke secondary to FMD (fibromuscular dysplasia)
- Stroke secondary to syphilis

**Prevention** [Return to top](#)

Stroke prevention involves controlling the risk factors. Treat hypertension, diabetes, heart disease, and other associated disorders. Reduce or stop smoking. A low-cholesterol, low-salt diet may be appropriate if the risk factors include atherosclerosis or hypertension. Exercise more.

The treatment of TIA can prevent some strokes.

**Symptoms** [Return to top](#)

- Loss of movement (paralysis) of any body area
- Weakness
- Decreased sensation
- Numbness
- Tingling or other sensation changes
- Decreased vision
- Language difficulties (aphasia):
  - slurred, thick, difficult speech
  - inability to speak
  - inability to understand speech
  - may have difficulty with reading or writing
- Inability to recognize or identify sensory stimuli (agnosia) resulting in "neglect" of one side of the body
- Loss of memory
- Vertigo (abnormal sensation of movement)
- Loss of coordination
- Swallowing difficulties
- Personality changes
- Mood/emotion changes (such as depression or apathy)
- Consciousness changes:
  - sleepy
  - stuporous/somnolent/lethargic
  - comatose/unconscious
- Urinary incontinence (lack of control over bladder)
- Lack of control over the bowels
- Cognitive decline
  - dementia
  - easily distracted
  - impaired judgment
  - limited attention

Additional symptoms that may be associated with this disease:

- Tongue problems
- Seizures
- Movement, unpredictable - jerky
- Movement, uncontrollable
- Movement, dysfunctional
- Incontinence
- Fatigue
- Fainting
- Facial paralysis

- Eye movements, uncontrollable
- Eye lid drooping
- Drooling
- Breathing, absent temporarily
- Behavior, unusual or strange
- Abnormal lack of sweating

Note: Specific changes in brain function (neurologic deficits) depend on the location and amount of injury to the brain. The symptoms are typically on one side of the body but may be isolated to specific functions, may involve one side of the body and the opposite side of the face, or may involve the face only.

#### Signs and tests [Return to top](#)

In diagnosing a stroke, the way the symptoms develop is important. The symptoms may be severe at the beginning of the stroke, or symptoms may progress or fluctuate for the first day or two (stroke in evolution). Once there is no further deterioration, the stroke is considered a complete stroke.

The exam will look for specific neurologic, motor, and sensory deficits, because these often correspond closely to the location of the injury to the brain. An examination may show changes in vision or visual fields, abnormal reflexes or abnormal extent of "normal" reflexes, abnormal eye movements, muscle weakness, decreased sensation, and other changes. A "bruit" (an abnormal sound heard with the stethoscope) may be heard over the carotid arteries of the neck. There may be signs of atrial fibrillation.

Tests may determine the location and cause of the stroke and rule out other disorders that can cause the symptoms:

- A head CT or MRI of head may be used to rule out bleeding (hemorrhage) or other lesions and define the location and extent of the stroke
- An ECG (electrocardiogram) may be used to determine underlying heart disorders
- An echocardiogram may be used if the cause is suspected to be cardiac embolus
- A carotid duplex (ultrasound) may be used if the cause is suspected to be carotid artery stenosis
- A cerebral (head) arteriography may be used if a disorder involving the blood vessels is suspected

This disease may also alter the results of the following tests:

- Platelet aggregation test
- Osmolality
- LDH isoenzymes
- LDH
- Cytometric study
- CSF collection
- CPK isoenzymes
- BERA (brainstem evoked response audiometry)

#### Treatment [Return to top](#)

A stroke is serious condition. Immediate treatment is required. The treatment varies depending on the severity of symptoms. For virtually all strokes, hospitalization is required, possibly including intensive care and life support.

There is no known cure for a stroke. The treatment involves rehabilitation (based on the symptoms) and prevention of future strokes. Recovery may occur as other areas of the brain take over functioning for the damaged areas. The goal of treatment is to prevent the spread of the stroke and to maximize the patient's ability to function.

#### IMMEDIATE TREATMENT

Life support and coma treatment are performed as needed.

A number of medications may be used. RTPA is a medicine that lyses the clot and potentially restores blood flow to the affected area to prevent cell death and permanent damage. However, there are strict criteria for who can receive RTPA -- most important is that the stroke victim be evaluated and treated by a specialized stroke team within 3 hours of onset of symptoms. It is a controversial medication because there is a risk of serious bleeding.

In appropriate circumstances, other anti-coagulants such as heparin and coumadin are used to prevent recurrent strokes. Aspirin and other anti-platelet agents are used to prevent strokes as well.

Analgesics may be needed to control severe headache. Anti-hypertensive medication may be needed to control high blood pressure.

Nutrients and fluids may be necessary, especially if the person has swallowing difficulties. The nutrients and fluids may be given through an intravenous tube or a tube in the stomach (feeding tube or gastrostomy tube). Swallowing difficulties may be temporary or permanent.

Surgery may be appropriate in some cases, including surgical removal of blood clots from the brain.

Carotid endarterectomy, removal of plaque from the carotid arteries, may help prevent new strokes from occurring in some people.

#### LONG-TERM TREATMENT

The recovery time and need for long-term treatment vary. Depression and other symptoms should be treated.

Speech therapy, occupational therapy, physical therapy, positioning, range of motion exercises, and other therapies may prevent complications and promote maximum recovery of function. People should stay active within their physical limitations.

In some cases, urinary catheterization or bladder/bowel control programs may be necessary to control incontinence.

The individual's safety must be considered. Some people with stroke appear to have no awareness of their surroundings on the affected side. Others show a marked indifference or lack of judgment, which increases the need for safety precautions. For these people, friends and family members should repeatedly reinforce important cues, like name, age, date, time, and where they live, to help reduce disorientation.

Communication may require pictures, demonstration, verbal cues, or other strategies, depending on the type and extent of language deficit.

In-home care, boarding homes, adult day care, or convalescent homes may be required to provide a safe environment, control aggressive or agitated behavior, and meet physiological needs.

Behavior modification may be helpful for some people in controlling unacceptable or dangerous behaviors. This consists of rewarding appropriate or positive behaviors and ignoring inappropriate behaviors (within the bounds of safety).

Family counseling may help in coping with the changes required for home care. Visiting nurses or aides, volunteer services, homemakers, adult protective services, and other community resources may be helpful.

Legal advice may be appropriate. Advance directives, power of attorney, and other legal actions may make it easier to make ethical decisions regarding the care of the person with organic brain syndromes such as stroke.

#### Support groups [Return to top](#)

American Stroke Association  
A Division of the American Heart Association  
7272 Greenville Avenue, Dallas, TX 75231  
<http://www.strokeassociation.org>

Toll free phoneline for stroke survivors and caregivers: 1-888-4STROKE

### Prognosis [Return to top](#)

Stroke is the third leading cause of death in developed countries. The outlook depends on the cause and extent of damage. Of those who survive a stroke, many have long-term disabilities, but some recover most or all function.

### Complications [Return to top](#)

- Pressure sores
- Permanent loss of movement or sensation of a part of the body
- Bone fractures
- Joint contractures
- Muscle spasticity
- Permanent loss of cognitive or other brain functions
- Disruption of communication, decreased social interaction
- Decreased ability to function or care for self
- Decreased life span
- Multi-infarct dementia
- Side effects of medications
- Aspiration
- Malnutrition
- Pain syndromes (reflex sympathetic dystrophy)

### Call your health care provider if [Return to top](#)

Go to the emergency room or call the local emergency number (such as 911) if you have symptoms of a stroke. Stroke requires immediate treatment.

**Update Date: 01/30/01**

Updated by: Galit Kleiner-Fisman, MD, Beth-Israel Deaconess Medical Center, Boston, MA. Review provided by VeriMed Healthcare Network.

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The address of this page is: <http://hsl.mcmaster.ca/tomflem/stroke.html>

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For more information, see: [Aphasia](#), also in the [Illness](#) section of this resource.

For more information, see: [Heart disease](#), also in the [Illness](#) section of this resource.

For more information, see: [Heart health](#) in the [Wellness](#) section of this resource.

- Cerebrovascular accident - [Stroke Information Guide](#) from the U.S. NINDS
- Cerebrovascular accident - [Heart & Stroke A-Z Guide](#) from the American Heart Association
- Cerebrovascular accident - [Heart and Stroke Foundation of Canada](#) reducing the toll of disability and death 🇨🇦
- Cerebrovascular accident - [Heart and Stroke Foundation of Alberta & NWT](#) fighting Canada's number one killers 🇨🇦
- Cerebrovascular accident - [Nebraska Stroke Foundation](#) basic information on stroke and rehabilitation
- Cerebrovascular accident - [Institute For Reparative Medicine and Vascular Surgery](#) heightening awareness of stroke
- Cerebrovascular accident - [StrokeCenter](#) from the Washington University School of Medicine, in St. Louis, MO
- Cerebrovascular accident - [A Strike Against Stroke](#) an article from *Scientific American*
- Cerebrovascular accident - [Take Wellness to Heart](#) about heart disease & stroke in women, from the AHA
- Cerebrovascular accident - [NI MAST](#) consensus statement on medical management of stroke
- Cerebrovascular accident - [Northern Ireland Chest Heart & Stroke Association](#) rehabilitation and prevention
- Cerebrovascular accident - [Stroke Prevention Council](#) stroke education for Southern California communities
- Cerebrovascular accident - [Rehabilitation for Strokes](#) Japanese-inspired English, but understandable, valuable insights
- Cerebrovascular accident - [Stroke and Aging Research Project Bibliography](#) from Columbia-Presbyterian Medical Center
- Cerebrovascular accident - [American Stroke Association](#) a division of the *American Heart Association*
- Cerebrovascular accident - [National Stroke Association](#) reducing the impact and the incidence of stroke
- Cerebrovascular accident - [StrokeHelp.com](#) practical therapeutic suggestions for those helping stroke survivors
- Cerebrovascular accident - [Stroke Information Directory](#) fact sheets, testing primers, clinical guidelines, and more

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Wallace Sife



Restorative Neurology  
Larry B. Goldstein

# STROKE



## Cerebrovascular Accident

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### A teaching presentation on Stroke

For families patients and rehabilitation team members

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